Remarks

Claims 7-22 were pending in the subject application. By this Amendment, claim 21 has been cancelled. The undersigned avers that no new matter is introduced by this amendment. Entry and consideration of the amendments presented herein is respectfully requested. It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of the applicant's agreement with or acquiescence in the Examiner's position. Accordingly, claims 7-20 and 22 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

Submitted herewith is a Request for Continued Examination (RCE) under 37 C.F.R. §1.114 for the subject application.

Claims 7-22 have been rejected under 35 U.S.C. §112, first paragraph, as lacking sufficient written description. The specification provides an adequate written description of the claimed subject matter, conveying to one of ordinary skill in the art that the applicant was in possession of the claimed invention at the time the application was filed.

By this Amendment, the applicant has cancelled claim 21, which was drawn to a sensor chip. Claims 7-20 and 22 are drawn to methods for sequencing a polynucleotide.

The subject specification provides relevant identifying characteristics sufficient to describe the claimed methods in such full, clear, concise, and exact terms that one of ordinary skill in the art would recognize that the applicant was in possession of the claimed invention. The Patent Office has the initial burden of presenting evidence or reasoning to explain why persons of ordinary skill in the art would not recognize in the original disclosure a description of the invention defined by the claims. *In re Wertheim*, 541 F.2d 257, 263; 191 USPQ 90, 97 (CCPA 1976). The applicant submits that the Examiner has not introduced sufficient evidence or technical reasoning to shift the burden of going forward with contrary evidence to the applicant.

The Office Action does not articulate **why** the subject specification does not provide an adequate written description of the claimed subject matter. At page 7, lines 26-28, the subject specification indicates that the DNA sequencing in the Example was conducted by the method

described in WO-A-99/05315, which is of record, using the apparatus shown there in Figure 1, but using only one focusing assembly for pulsing monochromatic light into the cell. Figure 1 of WO-A-99/05315 is a schematic illustration of polynucleotide sequence analysis using surface plasmon resonance (SPR) spectroscopy and a polymerase enzyme, and shows an SPR sensing system and fluidic cell (see page 14, lines 23-27, and page 15, lines 1-17, of WO-A-99/05315). The specification also makes it clear that conventional apparatus may be used in monitoring the changes in the enzyme. Although the example refers to a modified BIAcore 2000 system, any conventional SPR machine is suitable. The modification referred to in the Example is explained at page 7, line 26, of the subject specification, which states that the apparatus described in WO 99/05315 was used, but with only one focusing assembly (instead of two focusing assemblies). This modification was made because separate blocked nucleotides are not required in the method of the subject invention. Thus, there is no need for an additional focusing assembly.

Further description of the exemplified sequencing method is provided in the subsequent paragraphs of pages 7 and 8 of the subject specification. Step (ii) of claims 7, 14, and 22 of the subject application recites detecting the interaction between the enzyme and the nucleotide on the polynucleotide, to thereby determine the sequence of the target polynucleotide, the detection being carried out by measuring a change in, or absorption of, radiation that occurs during the interaction. As indicated at page 1, lines 28-33, and page 4, lines 16-21, of the subject specification, SPR is one technique by which a change in radiation or absorption of radiation can be measured. Experimental set ups for SPR, including SPR sensing systems and fluidic cells are well known in the art. As indicated above, any modification to established procedures that were made by the applicant are clearly described in the Example at pages 6-8 of the subject specification. Again, the Office Action has not provided reasons why adequate written description is lacking.

At page 8, the Office Action states that the specification fails to provide an adequate written description of the claimed helicases, and "one is not able to differentiate between helicases that are and are not encompassed by the claimed sensor chip." As indicated above, claim 21, which is drawn to a sensor chip, has been cancelled by this Amendment. Claims 7-20 and 22 are drawn to methods for sequencing a polynucleotide, using a helicase and/or primase. As taught at page 2, lines 29-33, and page 3, lines 1-34, of the subject specification, helicases and methods for their isolation have

been known for over twenty years and PcrA helicase is but one example that may be used in the invention. One skilled in the art can readily visualize and discern members of the recited class of enzymes, and how to obtain them. Thus, the subject specification provides a description of suitable enzymes, and methods for sequencing a polynucleotide using the enzymes, permitting a person of ordinary skill in the art to clearly recognize that the applicant had possession of the claimed invention.

> Use of known chemical compounds in a manner auxiliary to the invention must have a corresponding written description only so specific as to lead one having ordinary skill in the art to that class of compounds. *In re Herschler*, 591 F.2d 693, 697; 200 USPQ 711, 714 (CCPA 1979).

The Examiner has the initial burden of presenting evidence or reasoning to explain how there is substantial variation within the recited class of helicases such that one of ordinary skill in the art could not predict the operability in the invention of any species of helicases within the described class (see MPEP §2163 II A3(a)ii)—For each claim drawn to a genus). This the Examiner has not done. The Office Action does not indicate why the examples of helicases disclosed at page 2, lines 29-33; page 3; page 4, lines 1-5; and page 6, lines 25-31, of the subject specification are not representative of the recited genus of helicases.

At page 8, the Office Action makes the following statement regarding the helicases recited in the claims, "[c]learly, the specification does not reasonably suggest that applicant was in possession of that which has not yet even been discovered at this date, much less in possession of that which will be discovered 10 or 20 years hence." At page 11, the Office Action further states "the claimed invention fairly encompasses helicases that have not yet been discovered, much less been rendered well known. Accordingly, the specification does not and cannot adequately describe or enable that which has yet to be identified and characterized." As an initial matter, the applicant notes that the Office Action speculates that further helicases remain to be discovered or identified. This may or may not be the case. Regardless, the applicant respectfully submits that as long as the subject specification enables and provides a sufficient written description of the claimed subject matter as required by 35 U.S.C. §112, first paragraph, it is wholly irrelevant that the claimed methods encompass the use of materials yet to be identified. The test for sufficiency of enablement is whether the specification enables one of ordinary skill in the art to practice the invention without the need for

undue experimentation: *In re Wands*, 858 F.2d 731, 737; 8 USPQ2d 1400. The scope of enablement provided by the specification must only bear a reasonable correlation to the scope of the claims. The test for sufficiency of written description is whether the specification conveys with reasonable clarity to those skilled in the art that the applicant was in possession of the invention embraced by the claims. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-1564; 19 USPQ2d, 1111, 1117 (Fed. Cir. 1991). The filing date of an application is the date at which the sufficiency of enablement and written description are to be assessed. Thus, an applicant's conformance with 35 U.S.C. §112, first paragraph, is determined as of the effective filing date of a patent application, and not a subsequent time, such that an application need not enable, or provide written description for, claims construed to encompass subsequently arising ("future") technology. *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1325-26 (Fed. Cir. 2004); MPEP §§2163 and 2164.05(a).

At page 10, lines 1-3, the Office Action asserts that "there must be some correlation established between structure and function" and points out that the subject specification does not disclose any sequences of helicases. The applicant respectfully submits that the Federal Circuit has made it clear that a sequence need not appear in a specification drawn to biological subject matter when the state of the scientific knowledge includes such structural information. Helicase sequences of many organisms, and methods for isolating the enzymes, have been known in the art for several years. The descriptive text needed to meet the written description requirement varies with the nature and scope of the invention at issue, and with the scientific and technological knowledge already in existence. When the prior art includes the sequence information, legal precedent does not set a *per se* rule that the information must be determined afresh. There is no rule stating that in order to satisfy the written description requirement, known DNA or amino acid sequences must be disclosed in the specification. Rather, the written description requirement must be considered in the context of the claimed invention and the state of knowledge in the relevant art. *Capon et al. v. Eshhar et al.*, 418 F.3d, 1349 (Fed. Cir. 2005). In Capon *et al.*, which is a case stemming from a patent interference between two parties each claiming chimeric cell surface receptors, the U.S. Court of Appeals for the Federal Circuit struck down as "an inappropriate generalization" the Board of Patent Appeals and Interference's rule that, even where the nucleotide sequences of the component DNA are known, the nucleotide sequences of the chimeric genes must be fully presented. The Court noted

"[i]t is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention." As explained by the Court:

> Precedent illustrates that the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter ...

Enzymes that exhibit "helicase" function are well defined in the art, as are sequences that encode them. Those of ordinary skill in the art would readily envision and discern suitable helicases for use in the invention. It is not necessary for the applicant to define the recited class of helicases by any structure-function relationship.

The mere fact that various publications are cited within the specification without the content of those publications being incorporated by reference does not suggest or raise an inference that the claimed invention is not sufficiently described and enabled as required under 35 U.S.C. §112, first paragraph. Incorporation by reference is a convention by which an applicant, in the interest of economy of time and space, may incorporate certain types of documents by specific reference to such sources within the application. However, it is well settled that the specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public. *In re Buchner*, 929 F.2d 660, 661; 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). The description need only describe in detail that which is new or not conventional. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384; 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463; 221 USPQ 481, 489 (Fed. Cir. 1984). Furthermore, contrary to the generalizations made at pages 3 and 4 of the outstanding Office Action, the applicant can rely upon the disclosures of such publications for fulfillment of the requirements under 35 U.S.C. §112, first paragraph. The analysis of whether the specification complies with the written description requirement calls for the Examiner to compare the scope of the claim with the scope of the description to determine whether the applicant has demonstrated possession of the claimed invention. Such a review is conducted from the standpoint of one of ordinary skill in the art

at the time the application was filed (*Wang Labs. V. Toshiba Corp.*, 993 F2d. 858, 865; 26 USPQ2d 1767, 1774 (Fed. Cir. 1993)) and should include a determination of the field of the invention and the level of skill and knowledge in the art. Thus, the interpretation of what is disclosed in the application must be made in light of the knowledge of one skilled in the art. Indeed, there is generally an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement (see MPEP §2163 IIA2). Thus, prior publications can be relied upon to establish whether an art is mature and what was known to those skilled in the art at the time the application was filed. The Examiner's failure to consider these prior publications in relation to 35 U.S.C. §112, first paragraph, is improper.

The applicant's invention is based on a novel and non-obvious combination of well known materials and conventional techniques. The intricacies need not be detailed *ad absurdum*. The skill of the ordinary skilled person must be taken into account. *Merck & Co. v. Chase Chem. Co.*, 273 F.Supp. 68 (D.N.J. 1967). Further, where complexity dictates, broad terminology complies with the statute. *Application of Fuetterer*, 319 F.2d 259, 262 (1963); *Sears, Roebuck and Co. v. Jones*, 308 F.2d 705, 707, 708 (10th Cir. 1962).

The subject specification provides relevant identifying characteristics sufficient to describe the claimed invention in such full, clear, concise, and exact terms that one of ordinary skill in the art would recognize that the applicant was in possession of the claimed invention. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, for lack of written description, is respectfully requested.

Claims 7-22 have been rejected under 35 U.S.C. §112, first paragraph, as non-enabled by the subject specification. The applicant respectfully submits that the invention as currently claimed is reasonably enabled by the specification.

In order to make a rejection based on non-enablement, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, F.2d 1557, 1562; 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). This the Examiner has not done. The Office Action does not articulate **why**, in view of the specification, one of ordinary skill in the art would lack information as to how to immobilize a helicase to a suitable solid support and how to carry out SPR analysis, for example. The mere fact that materials and methods cited in a patent

application are not incorporated by reference does not shift the burden to the applicant to show that the patent application contains an enabling disclosure. To the extent they are applicable to the instant rejection under 35 U.S.C. §112, first paragraph, for lack of enablement, the applicant's foregoing remarks in response to the rejection for lack of written description are incorporated herein by reference in their entirety.

Given the teachings of the subject specification, and the knowledge of those skilled in the art, one of ordinary skill in the art would be able to make and use the invention without undue experimentation. The subject specification makes it clear that the method of the invention can be carried out by immobilizing helicase or primase enzymes on to a suitable substrate and monitoring the enzyme conformation by detecting changes in absorption of radiation that occur during the enzyme reaction. No undue experimentation would be required.

The subject specification makes it clear that a conventional apparatus may be used in monitoring changes in the enzyme. Although the Example refers to a modified BIAcore 2000 system, any conventional SPR machine may be used, for example. At page 7, lines 26-28, the subject specification indicates that the DNA sequencing in the Example was conducted by the method described in WO-A-99/05315, which is of record, using the apparatus shown there in Figure 1. The modification referred to in the Example is explained at page 7, line 26, of the subject specification, which states that the apparatus in WO-A-99/05315 was used, but with only one focusing assembly (instead of two focusing assemblies). This modification was made because separate blocked nucleotides are not required in the method of the present invention. Thus, there is no need for a second focusing assembly.

Again, further description of the exemplified sequencing method is provided in the subsequent paragraphs of pages 7 and 8 of the subject specification. Step (ii) of claims 7, 14, and 22 of the subject application recites detecting the interaction between the enzyme and the nucleotide on the polynucleotide, to thereby determine the sequence of the target polynucleotide, the detection being carried out by measuring a change in, or absorption of, radiation that occurs during the interaction. As indicated at page 1, lines 28-33, and page 4, lines 16-21, of the subject specification, SPR is one technique by which a change in radiation or absorption of radiation can be measured. Experimental set ups for SPR, including SPR sensing systems and fluidic cells are well known in the

art. Any modifications to established procedures that were made by the applicant are clearly described in the Example at pages 6-8 of the subject specification.

At page 10, lines 9-12, the Office Action asserts that "the specification is essentially silent as to how the multitude of helicases would be used in the claimed method, or would be affixed to a chip and still have their requisite functionality." The applicant respectfully submits that this is incorrect. The applicant's specification teaches a method for sequencing a polynucleotide by analyzing the conformational or kinetic interaction between a helicase or primase enzyme and a target polynucleotide, which is achieved by monitoring the changes in, or absorption of, electromagnetic or other radiation that occurs if the reaction proceeds (see page 2, lines 21-25, of the subject specification). Methods for monitoring changes in, or absorption, of radiation, such as SPR and nuclear magnetic resonance (NMR) are well known in the art. As taught at page 5, lines 17-33, of the subject specification, immobilization of helicase or primase enzymes on to a suitable substrate may be carried out using standard techniques for enzyme immobilization known in the art, such as dextran or N-hydroxysuccinamide ester-activated linkages. At page 6, lines 33-34, the subject specification indicates that immobilization of the helicase was carried out according to the method of Jonsson *et al.* (*Biotechniques*, 1991, 11:620-627), which is of record. Details regarding the immobilization of the helicase enzyme on the chip, including the volumes and concentrations of reactants that were utilized, are provided at page 7, lines 1-10, of the subject specification. Advantages of immobilization are described at page 5, lines 1-16, of the specification. Methods of immobilizing helicases and using them in the method of the invention are disclosed in the subject specification. The Office Action cites no reasons to doubt that helicases could be immobilized as taught in the specification without loss of enzyme function. In order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). A specification which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. §112, first paragraph, unless there is a reason to doubt the objective truth of the

statements contained therein which must be relied on for enabling support. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). As stated by the court,

> it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure. *In re Marzocchi*, 439 F.2d at 224, 169 USPQ at 370.

At page 10, lines 18-22, the Office Action notes that the contents of the Bird *et al.* (1998) publication was not incorporated by reference and suggests that the specification does not disclose a reproducible source of essential starting materials. The enablement requirement of 35 U.S.C. §112, first paragraph, does not require that the applicant reinvent the wheel. There is no need to inform the layman nor disclose what one of ordinary skill in the art already possesses.

> Paragraph 1 permits resort to material outside of the specification in order to satisfy the enablement portion of the statute because it makes no sense to encumber the specification of a patent with all the knowledge of the past concerning how to make and use the claimed invention. One skilled in the art knows how to make and use a bolt, a wheel, a gear, a transistor, or a known chemical starting material. The specification would be of enormous and unnecessary length if one had to literally reinvent and describe the wheel. *Amtel Corporation v. Information Storage Devices, Inc.*, 198 F.3d 1374; 53 USPQ2d 1225 (Fed. Cir. 1999).

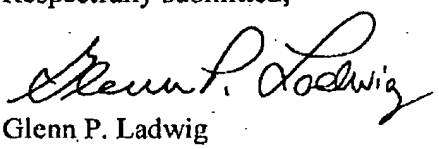
The applicant respectfully submits that the subject specification enables one of ordinary skill in the art how to make and use the invention without resort to undue experimentation. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, for lack of enablement, is respectfully requested.

In view of the foregoing remarks and amendments to the claims, the applicant believes that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

The applicant invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachments: Petition and Fee for Extension of Time
Request for Continued Examination (RCE) under 37 C.F.R. §1.114